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FINNEGAN, HENDERSON, FARABOW, GARRETT & DUNNER LLP
901 NEW YORK AVENUE, NW
WASHINGTON, DC 20001-4413

EXAMINER	
LOEWE, SUN JAE Y	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Application Number: 10/555,286
Filing Date: October 17, 2006
Appellant(s): JIMENEZ MAYORGA ET AL.

Almirall, S.A.
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed March 9, 2010 appealing from the Office action mailed January 16, 2009.

(2) Related Appeals and Interferences

The examiner is not aware of any related appeals, interferences, or judicial proceedings which will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

(3) Status of Claims

The statement of the status of claims contained in the brief is correct.

(4) Status of Amendments After Final

The examiner has no comment on the appellant's statement of the status of amendments after final rejection contained in the brief.

(6) Grounds of Rejection to be Reviewed on Appeal

The examiner has no comment on the appellant's statement of the grounds of rejection to be reviewed on appeal. Every ground of rejection set forth in the Office action from which the appeal is taken (as modified by any advisory actions) is being maintained by the examiner except for the grounds of rejection (if any) listed under the subheading "WITHDRAWN REJECTIONS." New grounds of rejection (if any) are provided under the subheading "NEW GROUNDS OF REJECTION."

(7) Claims Appendix

The examiner has no comment on the copy of the appealed claims contained in the Appendix to the appellant's brief.

(8) Evidence Relied Upon

Fukui et al., WO 2002014272

Patani et al., Chem. Rev., 96, 3147-3176

(9) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

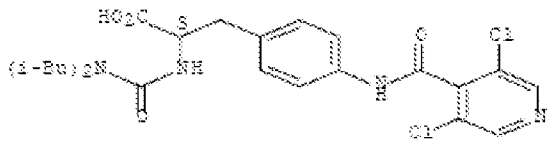
> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-10, 20 and 21 rejected under 35 U.S.C. 103(a) as being obvious over Fukui et al. (WO 2002014272) in view of Patani et al.

Determination of the scope and contents of prior art .
The reference teaches the following compound as a VLA-4 antagonist



Patani et al. teaches that sulfone (SO2) is a bioisostere of the carbonyl group. The reference teaches that sulfone moieties have been increasingly used as bioisosteres, and that the greater size associated with the sulfone moiety has been shown to be a factor that modulates biological activity (see pg. 3167).

Ascertaining the differences between prior art and instant claims.
The following modification to the prior art compound results in the instant elected species: replace carbonyl group (-CO-) with sulfone (SO2).

Resolving the level of ordinary skill in the pertinent art – Prima Facie Case of Obviousness.
One of ordinary skill would be motivated, from the disclosure in the prior art, to make the modification required to arrive at the instant invention with reasonable expectation of success for obtaining a compound with the same activity. The motivation to make the change would be to make additional compounds for the quoted purpose. The rationale relied upon is consistent with the guidelines of MPEP 2143.E., excerpts below:

> *E. "Obvious To Try" – Choosing From a Finite Number of Identified, Predictable Solutions, With a Reasonable Expectation of Success*
>
> To reject a claim based on this rationale, Office personnel must resolve the *Graham* factual inquiries. Then, Office personnel must articulate the following:
>
> (1) a finding that at the time of the invention, there had been a recognized problem or need in the art, which may include a design need or market pressure to solve a problem;
>
> (2) a finding that there had been a finite number of identified, predictable potential solutions to the recognized need or problem;
>
> (3) a finding that one of ordinary skill in the art could have pursued the known potential solutions with a reasonable expectation of success; and
>
> (4) whatever additional findings based on the *Graham* factual inquiries may be necessary, in view of the facts of the case under consideration, to explain a conclusion of obviousness.
>
> The rationale to support a conclusion that the claim would have been obvious is that "a person of ordinary skill has good reason to pursue the known options within his or her technical grasp. If this leads to the anticipated success, it is likely that product [was] not of innovation but of ordinary skill and common sense. In that instance the fact that a combination was obvious to try might show that it was obvious under § 103."

Thus, the instant claims are *prima facie* obvious over the teaching of the prior art.

(10) Response to Argument

Applicants have traversed the 35 USC 103 rejection. Applicants arguments and responses to those arguments are provided below, Sections a and b.

a) Applicant's arguments:

Applicants argue that the prior art does not provide any information which would lead one of ordinary skill in the art to select the cited compound.

Applicants state that the Examiner has not presented a reason why one of

ordinary skill would have selected the cited compound, out of dozens of other compounds disclosed in WO 2002/014272, as a lead compound. Applicants further argue that the section of the prior art referred to in the rejection shows IC50 of twenty four compounds, eleven of which are higher than that of the compound used in the rejection (see Table 1 on pg. 22 of Fukui et al.). Applicants conclude one of ordinary skill would not have any reason to select the cited compound as a lead for further modification.

Response to Applicant's arguments:

The prior art document provides 39 specific examples of VLA-4 antagonists. For 24 of these 39 specific examples, the IC50 data is provided. The compound used in the 35 USC 103 rejection, ie. Example 4, is one of the 24 embodiments for which IC50 data is provided. Further, Example 4 has IC50 of 4.7nM. This value is on the low end of the range reported for the 24 preferred embodiments – 0.014 nM being the lowest, and 99 nM being the highest. Therefore, the disclosure provides for one of ordinary skill to select Example 4 as a reasonable lead for further modification.

b) Applicant's arguments:

Applicants argue that the prior art fails to suggest the modification of carbonyl to sulfone. Applicant's support this argument by stating that the reference shows instances where carbonyl group replacement by sulfone

result in decreased activity. Applicants therefore conclude that the reference, rather than prompting one of ordinary skill to make the carbonyl to sulfone modification, discourages such a substitution.

Response to Applicant's arguments:

The prior art explicitly states that the sulfone moiety has increasingly been used as nonclassical divalent bioisosteres of the carbonyl group. In support, the prior art cites 6 references which show this replacement (ie. references 140-145 on pg. 3175). The references are for a variety of core structures for agents used in different pharmacological utilities: eg. anti-inflammatory tetrahydroisoquinolines; thiazole inhibitors of supreoxide production; purines used for anti-tumor agents, etc. Thus, the prior art explicitly suggests carbonyl to sulfone replacement as reasonable equivalents. Applicant's arguments that the prior art reference fails to suggest the modification of carbonyl to sulfone is not found to be persuasive as the reference explicitly suggests this modification as an alternate to the carbonyl group.

c) Applicant's arguments:

Applicants state that the Examiner has failed to show the required elements of an "obvious to try" rationale. Applicants state that to reject a claim based on an "obvious to try" rationale one must show that there is a recognized problem in the art that there are a number of identified predictable potential solutions to this problem.

Response to Applicant's arguments:

MPEP 2145.X.B states that an obvious to try rationale may support a conclusion that a claim would have been obvious where one skilled in the art is choosing from a finite number of identified, predictable solutions, with a reasonable expectation of success. A person of ordinary skill has good reason to pursue the known options within his or her technical grasp. The rationale applies to the current ground of rejection. One of ordinary skill has a reasonable expectation of success in producing a pharmacologically active compound with carbonyl to sulfone replacement. Furthermore, the reference of Patani et al. suggests certain bioisosteric replacements as a rational approach in drug design. This reference explicitly suggests carbonyl to sulfone replacement. Based on these facts, it is maintained that the rationale applied was proper.

(11) Related Proceeding(s) Appendix

No decision rendered by a court or the Board is identified by the examiner in the Related Appeals and Interferences section of this examiner's answer.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

/Sun Jae Y. Loewe/

Conferees:

/Joseph K. McKane/

Supervisory Patent Examiner, Art Unit 1626

/James O. Wilson/

Supervisory Patent Examiner, Art Unit 1624